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CURBSIDE CONSULT

Which Test Should I Order for an Inpatient Evaluation of Cardiac Ischemia?

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Abstract

Testing for cardiac ischemia, or for the obstructive coronary artery disease (CAD) that causes cardiac ischemia, is common among hospitalized patients. Many testing options exist. Choosing an appropriate test can be challenging and requires accurate risk stratification. Two major categories of testing are available: stress testing (also known as functional testing) and anatomical testing. Stress testing evaluates specifically for ischemia and can be conducted with or without imaging. Anatomical testing visualizes the obstructive CAD that causes ischemia. This article reviews how to choose an appropriate test for the evaluation of cardiac ischemia in the inpatient setting, using case examples to illustrate the considerations involved.

Introduction

Clinicians caring for patients in the hospital setting commonly consider noninvasive testing for cardiac ischemia or the obstructive coronary artery disease (CAD) that causes cardiac ischemia. In certain circumstances, such testing is clearly indicated — for example, in patients with stable chest pain symptoms that limit activity but with low suspicion of acute coronary syndrome. Rates of testing in the inpatient setting are inappropriately low for certain populations, such as those with new-onset heart failure.[1-3]

Many testing modalities are now available, and selecting the optimal test can be challenging. Although studies of ischemic evaluation in the inpatient setting are limited, applying evidence from the evaluation of acute chest pain in the emergency department (ED) or stable chest pain in the outpatient setting to the inpatient setting can offer insights.[4,5] There are two types of testing: stress testing (also known as functional testing), which directly assesses ischemia, and anatomical testing, which visualizes obstructive CAD.

Risk Stratification

The first step to evaluate for cardiac ischemia among hospitalized adults is to stratify patients as high, intermediate, or low cardiac risk (Fig. 1).[4-6] Features of high cardiac risk

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include angina at rest, malignant arrythmias (such as ventricular tachycardia or ventricular fibrillation), or cardiogenic shock. Patients with these features often have rapidly rising troponin levels and/or dynamic electrocardiogram (ECG) changes (e.g., ST elevations, ST depressions, or new left bundle branch block).[5,6] Recognizing these signs early is important, because patients with high-risk features often require urgent cardiac catheterization, and delayed time to procedure increases mortality.[7-10] Stress testing is contraindicated in patients with a high possibility of acute coronary syndrome because this type of testing may worsen ischemia.[4,11] Cardiology consultation is necessary.

Patients are considered to have low cardiac risk if the estimated 30-day risk of major adverse cardiovascular events or death is less than 1%, as described by studies in the outpatient and ED settings.[4,12,13] These patients generally do not benefit from further testing for cardiac ischemia.[5,12-14] Presenting features include nonischemic ECGs, negative serial troponins, and noncardiac-type chest pain. Characteristics of cardiac-type chest pain include substernal chest pressure that worsens with exertion and improves with rest or sublingual nitroglycerin. It may also present with pain to the neck, arm, or shoulder. Chest pain that is sharp, pleuritic, or burning is less likely to be from ischemia.

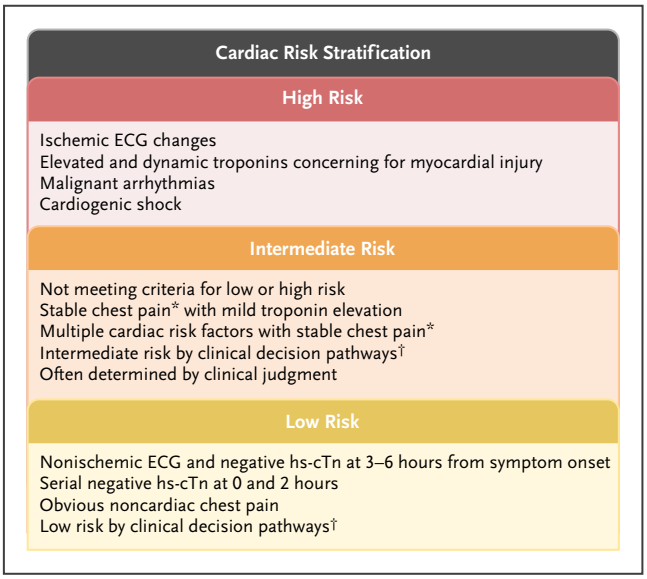
Cardiac Risk Stratification
High Risk
Ischemic ECG changes
Elevated and dynamic troponins concerning for myocardial injury
Malignant arrhythmias
Cardiogenic shock
Intermediate Risk
Not meeting criteria for low or high risk
Stable chest pain* with mild troponin elevation
Multiple cardiac risk factors with stable chest pain*
Intermediate risk by clinical decision pathways†
Often determined by clinical judgment
Low Risk
Nonischemic ECG and negative hs-cTn at 3–6 hours from symptom onset
Serial negative hs-cTn at 0 and 2 hours
Obvious noncardiac chest pain
Low risk by clinical decision pathways†

Figure 1. Cardiac Risk Stratification.
Presented are features suggestive of high, intermediate, or low cardiac risk. Patients with intermediate risk are often classified by clinical judgment. *Stable chest pain refers to symptoms present with activity, exertion, or stress. Stable chest pain should be reversible. Irreversible, persistent chest pain may be a concerning feature for high cardiac risk. †Clinical decision pathways were validated for emergency department presentations of acute chest pain. Clinician judgment should be applied when using them for inpatient settings. ECG denotes electrocardiogram; and hs-cTn, high-sensitivity cardiac troponins.

Clinical decision tools, such as the HEART (history, ECG, age, risk factors, and troponin) score,[15,16] ADAPT (2-hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker) protocol,[17] or high-sensitivity troponin–based approaches[14] have been validated for risk stratification in patients in the ED setting. Although intended for ED populations, they can be useful adjuncts to clinician judgment in the inpatient setting, especially because the included variables are of similar importance to inpatients and ED patients (e.g., ECG changes, troponin values, risk factors).

Patients with intermediate risk do not fit into either low- or high-risk categories and may benefit from further testing. For example, a patient may have levels of troponins that are indeterminate and intermittent chest pain. Alternatively, a patient could have higher-than-expected troponin elevation during acute illness without cardiac symptoms. These patients may have had a type II non-ST-segment elevation myocardial infarction due to demand ischemia, but if the suspicion of primary cardiac etiology remains, further testing for cardiac ischemia could be considered. Although many patients categorized as having intermediate cardiac risk may benefit from inpatient testing for cardiac ischemia, patients with nonischemic ECGs, negative troponins, and resolution of cardiac symptoms could be considered for outpatient evaluation. The decision of which patients to test as an inpatient versus as an outpatient is often driven by clinical judgment, and further studies in this area are necessary.

Testing Modalities for Patients at Intermediate Cardiac Risk

When evaluating for cardiac ischemia in patients considered to be of intermediate cardiac risk, clinicians can consider two categories of testing: stress testing and anatomical testing (Fig. 2).[18] Transthoracic echocardiography can be a useful adjunct for clinical decision-making in these patients, because it can provide information on cardiac function.

STRESS TESTING (FUNCTIONAL TESTING)

In patients undergoing stress testing, there are two key considerations: the approach to induce stress and the modality to assess ischemia. Stress can be applied with

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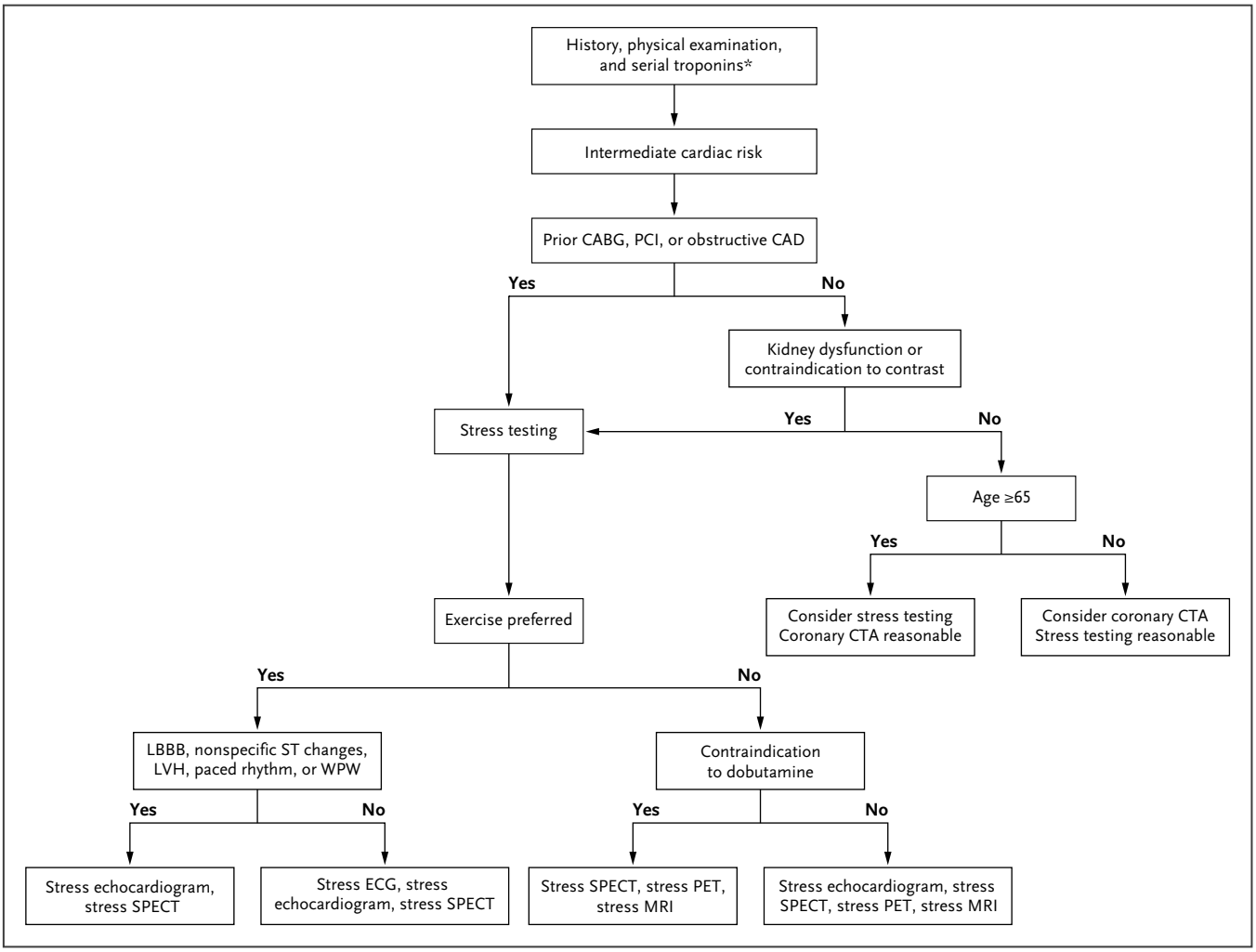

Figure 2. Selecting a Testing Modality.

Presented is a clinical decision approach to selecting a test for the inpatient evaluation of cardiac ischemia/obstructive CAD among patients with intermediate cardiac risk. In outpatient settings, exercise testing is often beneficial to get important clinical information about exercise capacity. However, for many hospitalized patients who are acutely ill, exercise testing may not be feasible, and thus pharmacologic therapy is a reasonable approach. Pharmacologic agents used for stress testing include vasodilators (adenosine, dipyridamole, regadenoson) and inotrope (dobutamine). Contraindications to vasodilators include sinus node dysfunction (without a pacemaker), high-degree heart block, low blood pressure (systolic blood pressure <90 mm Hg), caffeine use in the last 12 hours, and active wheezing or bronchoconstriction. Asthma, chronic obstructive pulmonary disease, and reactive airway disease are relative contraindications. Contraindications to inotropes include severe aortic stenosis, tachyarrhythmias, severe hypertension (>200/110 mm Hg), or active angina. Acute coronary syndrome is a contraindication for receiving stress agents. Select institutions may offer exercise myocardial perfusion with stress PET or MRI. CABG denotes coronary artery bypass graft; CAD, coronary artery disease; CTA, computed tomography angiography; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; MRI, magnetic resonance imaging; PCI, percutaneous coronary intervention; PET, positron emission tomography; SPECT, single-photon emission computed tomography; and WPW, Wolff–Parkinson–White syndrome. The asterisk (*) indicates that patients with intermediate cardiac risk should also be considered for transthoracic echocardiogram.

exercise (exercise stress testing) or medications (pharmacologic stress testing).

In the outpatient setting, the decision to exercise or use pharmacologic stress testing is determined by a patient's exercise capacity and functional capabilities: Would the patient be able to exercise safely to reach 85% of their maximum predicted heart rate — approximated by 85% × (220 – age)?[19] Patients who can exercise should generally undergo exercise stress testing.[19] Those who cannot

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should undergo pharmacologic stress testing. Acute illness and deconditioning in the inpatient setting may make exercise testing impractical.

Pharmacologic agents used for testing include vasodilators (adenosine, dipyridamole, regadenoson) and inotropes (dobutamine).[11] Absolute contraindications to vasodilators include sick sinus syndrome (without a pacemaker), high-degree heart block, low blood pressure (systolic blood pressure <90 mm Hg), and active wheezing or bronchoconstriction. Asthma, chronic obstructive pulmonary disease (COPD), and reactive airway disease that are not currently active are relative contraindications, although vasodilators can be considered in these patients after careful discussion with the stress-testing laboratory.[20,21] Caffeine use in the last 12 hours can negate testing and should be avoided. Absolute contraindications to inotropes include severe symptomatic aortic stenosis, tachyarrhythmias, severe hypertension (>180/100 mm Hg), or active angina.[20-22]

After selecting between exercise and pharmacologic stress testing, the next step is to decide the method of ischemia assessment (Table 1). In patients without baseline ECG abnormalities (e.g., ventricular paced rhythms, left ventricular hypertrophy, or bundle branch blocks) and with the ability to exercise, an exercise ECG stress test could be considered.[18] In exercise ECG stress testing, specific abnormalities in the ECG, such as downsloping ST depressions of more than 1 mm, indicate a positive test. Typical anginal symptoms, such as substernal chest discomfort that improves with rest, also indicate a positive study. Sensitivity and specificity of ECG stress testing are the lowest among ischemic testing modalities, at about 68% and 77%, respectively.[19]

Because exercise testing may not be an option for many hospitalized patients, an imaging-based stress test should generally be considered. Imaging modalities include echocardiography (stress echocardiogram), radionuclide myocardial perfusion imaging (stress single-photon emission computed tomography [SPECT] or stress positron emission tomography [PET]), and stress cardiac magnetic resonance imaging (MRI).[11,23]

Stress echocardiography can be performed with exercise or pharmacologic testing and avoids radiation.[24] The goal is to identify regional cardiac wall motion abnormalities induced during stress. Stress echocardiography can simultaneously assess for valvular disease and ejection fraction, both at rest and with exercise. The quality of testing can vary by center volume and expertise,[24] and image quality can be poor in select patients (such as those with COPD). Sensitivity and specificity for stress echocardiography are about 78% and 88%, respectively.[25]

Radionuclide myocardial perfusion imaging is the most readily available option for inpatient stress testing and historically has been a common test for hospitalized patients with intermediate cardiac risk. There are two types of imaging approaches for this testing: SPECT or PET.[26] In SPECT, technetium-99m–based radioisotopes are most commonly used, whereas in PET, rubidium-82 or ^{13}N-ammonia are common. Both imaging modalities can identify cardiac ischemia. PET has higher image quality and diagnostic accuracy compared with SPECT and can also assess coronary blood flow reserve, allowing for the evaluation of nonobstructive microvascular CAD.[26-28] PET requires less radiation than SPECT and produces higher-quality imaging but has a higher cost and is less readily available due to the specialized expertise required.[5] Both exercise and pharmacologic stress testing are options with SPECT, but generally only pharmacologic stress testing can be combined with PET (although development of exercise protocols is underway).[27] Sensitivity and specificity are about 91% and 89% for PET and 82% and 76% for SPECT, respectively.[29]

Stress cardiac MRI has become increasingly available[30] and uses non-radiation-based MRI to provide high-quality imaging of cardiac structure. The image quality of cardiac MRI is higher than that of exercise ECG, stress echocardiography, and SPECT and is similar to that of PET.[23,31,32] Often, stress testing can be coupled with evaluation of ventricular size and function, ascertainment of cardiac scarring, and detection of pericardial abnormalities.[30] Implanted devices such as pacemakers or internal cardiac defibrillators may be a relative barrier to this type of testing, although newer devices are increasingly MRI-compatible. Claustrophobia can also limit stress cardiac MRI, especially because scanning time is long.[24] Cardiac MRI is also more costly than other options such as stress echocardiography. Sensitivity and specificity are about 87% and 83%, respectively.[30]

ANATOMICAL TESTING

Coronary computed tomography angiography (CTA) is the recommended anatomical testing modality for patients at intermediate risk and uses contrast-enhanced imaging to

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Table 1. Inpatient Ischemic Evaluation Testing Modalities.*

Test	Summary	Stress (Functional) or Anatomical	Exercise or Pharmacologic Stress	Strengths	Limitations
Stress ECG	Patient exercises and is assessed for anginal symptoms or for dynamic ECG changes	Stress	Exercise only	• Low cost • High availability • No radiation exposure	• Not possible if patient is unable to exercise • Lower sensitivity and specificity • Cannot be used in patients taking digoxin or who have ECG abnormalities — LBBB, ST changes, V-paced rhythms, WPW, left ventricular hypertrophy
Stress echocardiogram	Patient exercises or receives pharmacologic therapy, with echocardiography used to assess for wall motion abnormalities	Stress	Exercise or pharmacologic	• Can assess for cardiac function, regional wall motion abnormalities, valvular abnormalities, pericardial effusions, and pulmonary hypertension • No radiation exposure	• Prior wall motion abnormalities can affect accuracy • Volume at local center can influence quality of examination • Image quality can vary • Dobutamine is only stress agent
Myocardial perfusion stress SPECT	Patient exercises or receives pharmacologic therapy, with nuclear imaging used to assess for perfusion defects	Stress	Exercise or pharmacologic	• High availability • Exercise option available among radionuclide testing • Fewer contraindications	• Lower imaging quality than PET • Radiation exposure
Myocardial perfusion stress PET	Patient receives pharmacologic therapy, with nuclear imaging used to assess for perfusion defects	Stress	Pharmacologic only	• Can assess coronary flow reserve (for microvascular dysfunction) • High spatial and temporal resolution • High sensitivity and specificity • Fewer contraindications	• Limited availability • High cost • Radiation exposure • Requires pharmacologic therapy
Myocardial perfusion stress MRI	Patient receives pharmacologic therapy, with MRI used to assess for perfusion defects	Stress	Pharmacologic only	• Can assess cardiac function, structure, pericardial disease, myocardial scarring • Can assess coronary flow reserve (for microvascular dysfunction) • High spatial and temporal resolution • No radiation exposure • High sensitivity and specificity	• Limited availability • High cost • Tolerability can be challenging in patients with claustrophobia due to long scan time • Cannot be used in patients with non-MRI-compatible pacemakers or implanted defibrillators
Coronary CTA	Cardiac computed tomography angiography scanning is gated to produce high-quality images of the coronary arteries, to assess for obstruction	Anatomical	NA	• Can assess for nonobstructive coronary artery disease • Can be an effective substitute for stress testing and does not require stress agent • Can be combined with fractional flow reserve to further assess the coronaries for flow-limiting disease	• Iodinated contrast use • Difficult to interpret for an acute event in patients with prior CABG, stenting, or known coronary artery disease • Can produce artifacts with significant coronary artery calcifications • Slower heart rates preferred (~60 BPM) • Avoid in patients with eGFR <30 ml/min/1.73 m^2

* This table provides a brief overview of considerations when ordering each type of testing. Many other strengths, limitations, and contraindications exist, and discussion with the testing laboratory staff can be useful before ordering the test. Pharmacologic agents used for stress testing include vasodilators (adenosine, dipyridamole, regadenoson) and inotrope (dobutamine). Contraindications to vasodilators include sinus node dysfunction (without a pacemaker), high-degree heart block, low blood pressure (systolic blood pressure <90 mm Hg), caffeine use in the last 12 hours, and active wheezing or bronchoconstriction. Asthma, chronic obstructive pulmonary disease, and reactive airway disease are relative contraindications. Contraindications to dobutamine include severe aortic stenosis, tachyarrhythmias, severe hypertension (>200/110 mm Hg), or active angina. Acute coronary syndrome is a contraindication for receiving stress agents. Select institutions may offer exercise with stress PET or MRI. BPM denotes beats per minute; CABG, coronary artery bypass graft; CTA, computed tomography angiography; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; LBBB, left bundle branch block; MRI, magnetic resonance imaging; NA, not applicable; PET, positron emission tomography; SPECT, single-photon emission computed tomography; V-paced, ventricular paced; and WPW, Wolff–Parkinson–White syndrome.

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provide noninvasive visualization of the coronary arteries.[4,33] Cardiac catheterization is an invasive anatomical testing modality that directly visualizes the coronary arteries. Clinical trials in the outpatient setting have demonstrated that coronary CTA is as effective as stress testing[34,35] and provides accuracy comparable with PET or stress cardiac MRI.[28,31,36]

Coronary CTA is recommended by the American Heart Association and American College of Cardiology for adults younger than 65 years of age,[4] because these patients are less likely to have severe coronary calcifications, which can affect test interpretation. Coronary CTA can be reasonable in many older patients as well.[37,38] A major benefit of coronary CTA among younger adults is the ability to identify nonobstructive CAD, allowing for an opportunity to prescribe preventive therapies. Evidence demonstrates higher uses of optimal medical therapy after coronary CTA than with stress testing, which can improve cardiovascular outcomes.[35,39] Coronary CTA is now often combined with fractional flow reserve, a technique to quantify coronary blood flow decreases among identified vessels with CAD.[33,40] Sensitivity and specificity for coronary CTA are about 95% and 79%, respectively.[36]

Contraindications to coronary CTA include severe kidney dysfunction (estimated glomerular filtration rate <30 ml/min/1.73 m^2) and an allergy to contrast.[5] Heart rates near 60 beats per minute maximize image quality, with reduced image quality for patients with tachyarrhythmias (e.g., atrial fibrillation). Use of beta blockers and nitroglycerin may enhance image quality. Patients with a prior history of multivessel CAD or prior stents are not ideal candidates for coronary CTA, because it can be difficult to distinguish between prior obstructive disease and more recent obstructive disease.[4,41]

Case Examples

Two case scenarios can help illustrate the decision points.

CASE 1

A 55-year-old man with hypertension and a history of smoking is hospitalized with a gastrointestinal bleed. Endoscopy does not show a clear etiology, and the bleeding resolves. He is thought to be ready for discharge on hospital day 6 but substernal chest pressure develops while he is walking around the floor. The chest pain lasts for 3 minutes and resolves with rest. He attempts to work with physical therapy later in the day and has similar chest pain with exertion that again resolves with rest. An ECG does not show signs of ischemia. He has a mild high-sensitivity troponin T increase to 75 ng/l (normal values, 0 to 14 ng/l) 3 hours after the episode, which subsequently decreases to normal levels. He has normal kidney function, and his hemoglobin level is stable and similar to baseline.

This patient's story has features consistent with cardiac-type chest pain (substernal and associated with activity). He has multiple risk factors, including hypertension, smoking history, and mild troponin elevation, which classify him as intermediate risk. He has no symptoms at rest or ischemic ECG changes to categorize him as high-risk.

Because he has multiple risk factors and is younger than 65 years of age, coronary CTA could be considered to identify obstructive CAD. An added benefit of this approach would be the potential to identify nonobstructive CAD, allowing for use of targeted preventive therapies. Stress testing would be reasonable, and stress ECG, echocardiogram, SPECT, PET, and stress cardiac MRI are all options. Given his stability, exercise testing could be considered, although with his recent illness, pharmacologic testing may be more feasible. Stress cardiac MRI, stress PET, or coronary CTA would have the highest diagnostic accuracy but at increased costs, and guidelines equally recommend the lower-cost options.[4]

CASE 2

A 76-year-old man with hypertension, hyperlipidemia, chronic kidney disease, and sick sinus syndrome (with a pacemaker implanted) is admitted for elective spine surgery. Postoperatively, he develops intermittent substernal chest pressure. These episodes last about 5 minutes and occur when he has severe lower back pain or mildly elevated blood pressures. He is given sublingual nitroglycerin during one episode, with improvement in symptoms. An ECG is obtained showing T wave flattening but no clear ischemic changes. He is receiving his home anginal therapy. He has increased high-sensitivity troponins initially that peak at 65 ng/l (normal values, 0 to 14 ng/l). He has an acute kidney injury with estimated glomerular filtration rate of 28 ml/min/1.73 m^2. His blood pressure is optimized, and he has no signs of acute bleeding, appears euvolemic on examination, and is otherwise near discharge.

This patient has multiple cardiac risk factors. He has features suggestive of cardiac chest pain because the

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discomfort is substernal, associated with activity, and improves with sublingual nitroglycerin. He is intermediate risk because he does not have high-risk features such as ischemic ECG changes, dynamic troponin elevations, rest symptoms, or signs of clinical heart failure.

In this setting, stress testing is favored. A coronary CTA is contraindicated because of his renal function, and a cardiac MRI may not be feasible if the patient's pacemaker is not MRI-compatible. Because of his recent back surgery, pharmacologic testing, rather than exercise testing, would be needed. A stress echocardiogram, stress SPECT, or stress PET would be reasonable.

Conclusions

Patients at intermediate cardiac risk can be considered for inpatient assessment of cardiac ischemia, with options including anatomical testing with coronary CTA or stress testing with stress ECG, echocardiography, SPECT, PET, or MRI. Many factors can affect the choice of optimal testing, although often multiple options are reasonable for most patients.

Disclosures

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